Tetrachloroethylene (CASRN 127-18-4)

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Tetrachloroethylene; CASRN 127-18-4

Health assessment information on a chemical substance is included in IRIS only after a comprehensive review of chronic toxicity data by U.S. EPA health scientists from several Program Offices and the Office of Research and Development. The summaries presented in Sections I and II represent a consensus reached in the review process. Background information and explanations of the methods used to derive the values given in IRIS are provided in the Background Documents.

STATUS OF DATA FOR Tetrachloroethylene

File First On-Line 01/31/1987

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	03/01/1988
Inhalation RfC Assessment (I.B.)	no data	
Carcinogenicity Assessment (II.)	no data	

_I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

_I.A. Reference Dose for Chronic Oral Exposure (RfD)

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Last Revised -- 03/01/1988

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other

sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

__I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Hepatotoxicity in mice, weight gain in rats 6-Week Mouse Gavage Study Buben and O'Flaherty, 1985	NOAEL: 20 mg/kg/day (converted to 14 mg/kg/day) LOAEL: 100 mg/kg/day (converted to 71 mg/kg/day)	1000	1	1E-2 mg/kg/day

*Conversion Factors: Doses have been adjusted for treatment schedule (5 days/week)

__I.A.2. Principal and Supporting Studies (Oral RfD)

Buben, J.A. and E.J. O'Flaherty. 1985. Delineation of the role of metabolism in the hepatotoxicity of trichloroethylene and perchloroethylene: a dose- effect study. Toxicol. Appl. Pharmacol. 78: 105-122.

Buben and O'Flaherty (1985) exposed Swiss-Cox mice to tetrachloroethylene in corn oil by gavage at doses of 0, 20, 100, 200, 500, 1500, and 2000 mg/kg, 5 days/ week for 6 weeks. Liver toxicity was evaluated by several parameters including liver weight/body weight ratio, hepatic triglyceride concentration, DNA content, histopathological evaluation, and serum enzyme levels. Increased liver triglycerides were first observed in mice treated with 100 mg/kg. Liver weight/body weight ratios were significantly higher than controls for animals treated with 100 mg/kg. At higher doses, hepatotoxic effects included decreased DNA content, increased SGPT, decreased levels of G6P and hepatocellular necrosis, degeneration and polyploidy.

A NOEL of 14 mg/kg/day was established in a second study, as well (Hayes et al., 1986). Groups of 20 Sprague-Dawley rats of both sexes were administered doses of 14, 400, or 1400 mg/kg/day in drinking water. Males in the high-dose group and females in the two highest groups exhibited depressed body weights. Equivocal evidence of hepatotoxicity (increased liver and kidney weight/body weight ratios) were also observed at the higher doses.

__I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF -- The uncertainty factor of 1000 results from multiplying factors of 10 to account for intraspecies variability, interspecies variability and extrapolation of a subchronic effect level to its chronic equivalent.

MF -- None

__I.A.4. Additional Studies/Comments (Oral RfD)

Other data support the findings of the principal studies. Exposure of mice and rats to tetrachloroethylene by gavage for 11 days caused hepatotoxicity (centrilobular swelling) at doses as low as 100 mg/kg/day in mice (Schumann et al., 1980). Mice

Quantitative Estimate of Carcinogenic Risk from Oral Exposure
- Summary of Risk Estimates
- Dose-Response Data
- Additional Comments
- Discussion of Confidence

Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure
- Summary of Risk Estimates
- Dose-Response Data
- Additional Comments
- Discussion of Confidence

EPA Documentation, Review and, Contacts
- Bibliography
- Revision History
- Synonyms

were more sensitive to the effects of tetrachloroethylene exposure than rats. Increased liver weight was observed in mice at 250 mg/kg, while rats did not exhibit these effects until doses of 1000 mg/kg/day were reached. Relative sensitivity to man cannot be readily established but the RfD of 1E-2 mg/kg/day is protective of the most mild effects observed in humans [diminished odor perception/modified Romberg test scores in volunteers exposed to 100 ppm for 7 hours; roughly equivalent to 20 mg/kg/day (Stewart et al., 1961)].

The principal studies are of short duration. Inhalation studies have been performed which indicate that the uncertainty factor of 10 is sufficient for extrapolation of the subchronic effect to its chronic equivalent. Liver enlargement and vacuolation of hepatocytes were found to be reversible lesions for mice exposed to low concentrations of tetrachloroethylene (Kjellstrand et al., 1984). In addition, elevated liver weight/body weight ratios observed in animals exposed to tetrachloroethylene for 30 days were similar to those in animals exposed for 120 days. Several chronic inhalation studies have also been performed (Carpenter, 1937; NTP, 1985; Rowe et al., 1952). None are inconsistent with a NOAEL of 14 mg/kg/day for tetrachloroethylene observed by Buben and O'Flaherty (1985) and Hayes et al. (1986).

__I.A.5. Confidence in the Oral RfD

Study -- Low
Database -- Medium
RfD -- Medium

No one study combines the features desired for deriving an RfD: oral exposure, large number of animals, multiple dose groups, testing in both sexes and chronic exposure. Confidence in the principal studies is low mainly because of the lack of complete histopathological examination at the NOAEL in the mouse study. The database is relatively complete but lacks studies of reproductive and teratology endpoints subsequent to oral exposure; thus, it receives a medium confidence rating. Medium confidence in the RfD follows.

__I.A.6. EPA Documentation and Review of the Oral RfD

U.S. EPA. 1985. Health Assessment Document for Tetrachloroethylene (Perchloroethylene). Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC for the Office of Air Quality Planning and Standards, Research Triangle Park, NC. EPA 600/8-82/005F.

U.S. EPA. 1987. Quantification of Toxicological Effects for Tetrachloroethylene. Prepared from the Health Assessment Document for Tetrachloroethylene (Perchloroethylene). Office of Drinking Water, Washington, DC.

Agency Work Group Review -- 05/20/1985, 08/05/1986, 09/17/1987

Verification Date -- 09/17/1987

__I.A.7. EPA Contacts (Oral RfD)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

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_I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

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Not available at this time.

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_II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name -- Tetrachloroethylene
CASRN -- 127-18-4

Not available at this time.

_VI. Bibliography

Substance Name -- Tetrachloroethylene
CASRN -- 127-18-4
Last Revised -- 07/01/1989

_VI.A. Oral RfD References

Buben, J.A. and E.J. O'Flaherty. 1985. Delineation of the role of metabolism in the hepatotoxicity of trichloroethylene and perchloroethylene: A dose- effect study. Toxicol. Appl. Pharmacol. 78: 105-122.

Carpenter, C.P. 1937. The chronic toxicity of tetrachloroethylene. J. Ind. Hyg. Toxicol. 19(7): 323-336.

Hayes, J.R., L.W. Condie, Jr. and J.F. Borzelleca. 1986. The subchronic toxicity of tetrachloroethylene (perchloroethylene) administered in the drinking water of rats. Fund. Appl. Toxicol. 7: 119-125.

Kjellstrand, P., B. Holmquist, M. Kanje, et al. 1984. Perchloroethylene: Effects on body and organ weights and plasma butyrylcholinesterase activity in mice. Acta Pharmacol. Toxicol. 54(5): 414-424.

NTP (National Toxicology Program). 1985. NTP Technical Report on the Toxicology and Carcinogenesis Studies of Tetrachloroethylene (perchloroethylene). U.S. Dept. Health and Human Services, NIH Publ. No. 85- 2567.

Rowe, V.K., D.D. McCollister, H.C. Spencer, E.M. Adams and D.D. Irish. 1952. Vapor toxicity of tetrachloroethylene for laboratory animals and human subjects. Arch. Ind. Hyg. Occup. Med. 5: 566-579.

Schumann, A.M., J.F. Quast and P.G. Watanabe. 1980. The pharmacokinetics and macromolecular interaction of perchloroethylene in mice and rats as related to oncogenicity. Toxicol. Appl. Pharmacol. 55: 207-219.

Stewart, R.D., H.H. Gay, D.S. Erley, C.L. Hake and A.W. Schaffer. 1961. Human exposure to tetrachloroethylene vapor. Arch. Environ. Health. 2: 40-46.

U.S. EPA. 1985. Health Assessment Document for Tetrachloroethylene (perchloroethylene). Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC for the Office of Air Quality Planning and Standards, Research Triangle Park, NC. EPA 600/8-82-005F. Office of Drinking Water, Washington, DC.

U.S. EPA. 1987. Quantification of Toxicological Effects for Tetrachloroethylene. Prepared from the Health Assessment Document for Tetrachloroethylene (perchloroethylene). Office of Drinking Water, Washington, DC.

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_VI.B. Inhalation RfC References

None

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_VI.C. Carcinogenicity Assessment References

None

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_VII. Revision History

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Date	Section	Description
12/23/1987	I.A.	RfD withdrawn pending further review
03/01/1988	I.A.	Revised Oral RfD sumary added - RfD changed
03/01/1988	III.A.	Health Advisory added
07/01/1989	VI.	Bibliography on-line
05/01/1990	II.	Carcinogen assessment now under review
06/01/1990	IV.A.1.	Area code for EPA contact corrected
06/01/1990	IV.F.1.	EPA contact changed
01/01/1992	IV.	Regulatory actions updated
04/01/1992	IV.	Regulatory action section withdrawn
08/01/1995	II.	EPA's RfD/RfC and CRAVE workgroups were discontinued in May, 1995. Chemical substance reviews that were not completed by September 1995 were taken out of IRIS review. The IRIS Pilot Program replaced the

		workgroup functions beginning in September, 1995.
04/01/1997	III., IV., V.	Drinking Water Health Advisories, EPA Regulatory Actions, and Supplementary Data were removed from IRIS on or before April 1997. IRIS users were directed to the appropriate EPA Program Offices for this information.
01/02/1998	I., II.	This chemical is being reassessed under the IRIS Program.

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_VIII. Synonyms

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127-18-4
Ankilostin
Antisal 1
Antisol 1
Carbon bichloride
Carbon dichloride
Czterochloroetylen
Dee-Solv
Didakene
Didokene
Dowclene EC
Dow-Per
ENT 1,860
Ethene, tetrachloro-
Ethylene tetrachloride
Ethylene, tetrachloro-
Fedal-Un
NCI-C04580
Nema
PCE
PER
Perawin
PERC
Perchloorethyleen, per
Perchlor
Perchloraethylen, per
Perchlorethylene
Perchlorethylene, per
Perchloroethylene
Perclene
Percloroetilene
Percosolv
Percosolve
PERK
Perklone
Persec
Tetlen

Tetracap
Tetrachlooretheen
Tetrachloraethen
Tetrachlorethylene
Tetrachloroethene
Tetrachloroethylene
1,1,2,2-Tetrachloroethylene.
Tetracloroetene
Tetraguer
Tetraleno
Tetralex
Tetravec
Tetroguer
Tetropil
WLN: GYGUYGG

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